REMARKS

Claims 1-6 and 8-24 are pending in this application. Claims 2-4, 9-10, 12, 14-15, 18-19, 21 and 23-24 have been withdrawn from consideration as drawn to a non-elected invention. Claim 1 has been amended to correct a typographical error. Claims 9-10, 12, 14-15, 18-19, 21 and 23-24 are canceled by this Amendment to make this Request for Consideration a complete reply to the Final Office Action. Also included herewith is a Notice of Appeal.

The amendments to the claims are supported by the application as originally filed, do not add new matter, and are otherwise proper. Applicants respectfully request entry of this Amendment in its entirety. In view of the following remarks, applicants respectfully request reconsideration of the claims and submit that the application is in condition for allowance. This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier.

Withdrawal of Claims

In the Office Action, independent claim 1 and claims 8, 11 and 13 dependent thereon were withdrawn from consideration as directed to non-elected inventions. Specifically, the Office Action stated that "[c]laim 1, as amended, is directed to an invention that is independent or distinct from the invention claimed for the following reasons: claim 1 recites a composition comprising a peptide of SEQ ID NO:9." Applicants respectfully disagree with the withdrawal of these claims for the following reasons. First, "[t]he use of sequence identification numbers (SEQ ID NO:X) **only** provides a **shorthand** way for applicants to discuss and claim their inventions. These identification numbers **do not** in **any** way **restrict** the manner in which an invention can be claimed." MPEP§ 2422.03 (emphasis added). Applicants originally elected examination of the peptide comprising the sequence W-S-A_1-C-S-A_2-C-G. Applicants did not elect SEQ ID NO:1 because sequence identifiers are artificial devices used for identification purposes only as is made clear by the above MPEP section. The currently claimed peptide Y–W-

S-A_1-C-S-A_2-C-G–Z has the exact same peptide sequence previously set forth in the claim and simply specifies the terminal ends of the peptide molecule. Moreover, the peptide selected as the single molecular embodiment for examination purposes, W-S-X_1-W-S-X_3-C-S-A_2-C-G (designated SEQ ID NO:7 for identification purposes only), also can clearly fall within the currently claimed peptide, as shown in the following table:

peptide												SEQ ID NO:
	W	S	A_1*				C	S	A_2*	C	G		1
Y^{Ψ}	W	S	A_1*				C	S	A_2*	C	G	Z^{Ψ}	9
	W	S	X_1^{δ}	W	S	X_3^{δ}	C	S	A_2*	C	G		7

* - A_1 and A_2 are amino acid sequences comprising 1 to 5 amino acids;

$^{\Psi}$ - Y and Z are (a) N- and C- terminal ends of the peptide, (b) amino acid chains having less than 6 amino acids, or (c) chains of compounds which are not amino acids; and

$^{\delta}$ - X_1 and X_3 are independently selected from G, S and C.

Accordingly, it is unreasonable to withdraw claims 1, 8, 11 and 13 from consideration because they have has the same salient features as the previously pending claims. It is readily apparent that that the new sequence identifier was only required because of the artificial sequence identifier rules. By withdrawing the current claims 1, 8, 11 and 13 the Office Action has restricted the manner in which the applicants choose to claim their invention based solely on sequence identifiers. This is against the express rule set forth in the MPEP that "identification numbers **do not** in **any** way **restrict** the manner in which an invention can be claimed." MPEP § 2422.03 (emphasis added). Accordingly, applicants respectfully request the Examiner examine independent claim 1 and claims 8, 11 and 13 dependent thereon.

Election/Restrictions

The Office Action also noted that "because the elected protein comprising SEQ ID NO:7 , which is a species of SEQ ID NO: 1, was known in prior art before the instant invention was made, it cannot serve as a unifying special technical feature. Accordingly, the claims are restricted based on the current US practice." Applicants respectfully disagree with this statement. The peptide selected as the single molecular embodiment for examination purposes set forth in claim 5, which contains the sequence W-S-X_1-W-S-X_3-C-S-A_2-C-G, can

serve as a unifying special technical feature because the presently claimed peptide was not known in the prior art. Specifically, the peptide sequence set forth in claim 5 ultimately depends from claim 1 which specifies the terminal ends of the peptide molecule as N- and C- terminal ends of the peptide, amino acid chains having less than 6 amino acids, or chains of compounds which are not amino acids and is not found in the cited art. The longest amino acid chain length the claimed peptide can have is 26 amino acids. For example, see the sequence Y-W-S-A_1-C-S-A_2-C-G-Z set forth in claim 1 where Y and Z are 5 amino acids ("Y and Z comprise... amino acid chains having less than 6 amino acids"), and A_1 and A_2 are 5 amino acids ("wherein A_1 and A_2 are amino acid sequences comprising 1 to 5 amino acids") which gives 5+1+1+5+1+1+5+1+1+5=26 amino acids. In contrast, Gobron *et al.*, cited as anticipating the claimed invention, only discloses a much longer peptide sequence. Because the claimed peptide is not disclosed in Gobron *et al.* it serves as a unifying special technical feature and applicants respectfully request examination of claims 1, 2-4, 9-10, 12, 14-15, 18-19, 21 and 23-24.

The Office Action also states that claims 5 and 6 were not considered "because claims 3 and 4, as originally filed, do not recite elected sequences SEQ ID NO:7 or 8." Applicants respectfully disagree with this statement. Again, applicants elected a peptide sequence for examination, not an artificial sequence identifier. The sequences set forth in claims 3 and 4 clearly cover the elected peptides as set forth in the following table:

peptide												Claim
Y^{ψ}	W	S	A_1*				C	S	A_2*	C	G	Z^{ψ}	1
	W	S	Pro or				C	S	A_2*	C	G		2
			X_1^{δ}	W	X_2^{δ}	X_3^{δ}							
	W	S	X_1^{δ}	W	S	X_3^{δ}	C	S	A_2*	C	G		3
	W	S	X_1^{δ}	W	S	X_3^{δ}	C	S	A_2*	C	G		5
	W	S	A_1*				C	S	R-S or V-S or V-T	C	G		4
	W	S	G	W	S	S	C	S	R	S	C	G		6

* - A_1 and A_2 are amino acid sequences comprising 1 to 5 amino acids;

$^{\psi}$ - Y and Z are (a) N- and C- terminal ends of the peptide, (b) amino acid chains having less than 6 amino acids, or (c) chains of compounds which are not amino acids; and

$^{\delta}$ - X_1 and X_3 are independently selected from G, S and C.

Thus, the statement in the Office Action that "claims 3 and 4, as originally filed, do not recite the elected sequences SEQ ID NO: 7 or 8" is clearly erroneous and claims 3 and 4 should be considered. Claim 2 should also be considered because the sequence set forth therein covers the elected peptide. Again, the Office Action appears to ignore the subject matter set forth in the claims and only improperly restricting examination of the invention by considering the invention only in terms of the artificial sequence identifiers.

Claim Objections

Claims 5 and 6 were objected to because they "depend from non-elected claims." As set forth above, the claims from which claim 5 and 6 depend cover the elected embodiments. Accordingly, applicants respectfully request the Examiner withdraw this objection.

Claim Rejections 35 U.S.C. §101

Applicants acknowledge the withdrawal of the rejection of claims 5, 6, 17, 20 and 22 under 35 U.S.C. §101 as lacking utility.

Claims 5, 6 and 16 were again "rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons" set forth in the previous Office Action. The previous Office Action stated "[t]he claims fail to include any limitations, which would distinguish the claimed proteins, peptides and compositions form those, which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are non-statutory subject matter." Applicants respectfully submit that this rejection is based on a misunderstanding of the currently claimed invention. As discussed above, the peptide selected as the single molecular embodiment for examination purposes set forth in claim 5 specifies the terminal ends of the peptide molecule because it is dependent on claim 1, as amended, which provides that the peptide has an amino acid chain length of no more than 26 contiguous amino acids. Claims 6 and 16 also include the terminal ends as set forth in claim 1. The claimed termini of the peptides distinguish them from naturally occurring peptides. Therefore, applicants respectfully request the Examiner with draw this rejection.

Claim Rejections – 35 U.S.C. §112

In the Office Action claims 17 and 20 were again "rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement for reasons of record[.]" Applicants respectfully traverse this rejection.

Several factors should be considered when determining whether claims are enabled by a disclosure. "These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention

based on the content of the disclosure." MPEP §2164.01.

Applicants respectfully submit that the present claims are enabled after weighing all of these factors. A discussion of these factors is set forth below. Applicants note that the enablement of each of the claims must be weighed individually.

Claim 17 is directed to a pharmaceutical composition comprising a peptide assigned SEQ ID NO:8. Applicants first note that claim that sets forth the identity of the peptide in the pharmaceutical composition was not rejected as non-enabling. It would be a trivial matter for one skilled in the art to formulate a specified peptide into a pharmaceutical formulation. All that is required to enable such an invention is knowledge of the peptide and a general understanding of pharmaceutical formulation. Nothing else is required to enable the formulation of claim 17. Accordingly little, if any, experimentation would be required to enable claim 17 and applicants respectfully request the Examiner withdraw this rejection with respect to claim 17.

Claim 20 is directed to a method of treating a pathological condition or trauma requiring the regeneration of nervous system cells using the peptide assigned SEQ ID NO:8. The level of ordinary skill in the art in the treatment and neurological arena is quite high. Although, the Office Action states there is a "lack of teaching[] and unpredictability of the art[,]" the unpredictability in the art revolves almost wholly, if not entirely, around identifying a compound or peptide that actually works in treatment. The unpredictability in the art does not revolve around the administration of the compound. The present inventors have provided working examples that demonstrate the claimed peptides not only lead to the aggregation of neurons but also neuritic growth and elongation *in vitro*. See, e.g., Examples 1 and 2. These examples also provide examples of dosages at which the peptides are effective in promoting nerve regeneration and/or growth. Accordingly, there is not a "total absence of working examples" in the present specification as put forward in the Office Action. The declaration submitted in response to the previous Office Action also shows the activity of the claimed peptide *in vivo*.

After the compound or peptide has been identified then it is a trivial matter for one skilled in the art to effectively administer a compound because the routes for administering compounds are not only known to those skilled in the art they are often limited and dictated by the injury and/or compound involved. It is also easy to determine an effective dose for any given

compound without resorting to undue experimentation. Despite this, the present application provides substantial guidance regarding the use and administration of the claimed peptides. For example, the present application references several articles and patent publications that provide peptides and compounds that have related activities and methods of treatment using these compounds. See, for example, EP 0443404 and Klar *et al.* Cell 69: 95-110 (1992). The present specification also provides guidance on routes of administration and targets for administration of the disclosed peptides. Page 6, lines 30-39.

In fact, the data set forth in the declaration provided in response to the previous Office Action clearly demonstrates that the skilled artisan could perform the method of treatment in claim 20 without undue experimentation. In the experiment described in the declaration, the claimed peptide was administered to a spinal cavity defect in a collagen device. This experiment clearly showed that the present peptide promoted nerve fiber regeneration. No regeneration was observed in a control experiment. The experiment described in the declaration did not require any special or unusual experimental techniques or undue experimentation. Undoubtedly, the performance of this successful technique would indisputably be well within the capability of a skilled artisan.

Despite this evidence, the Office Action stated that:

> [t]he limited working examples in the specification, as originally filed, pertain to in vitro studies of the instant peptides and cell cultures. Thus, the applicants' invention is predicated on the assertion that the peptide of SEQ ID NO:8 would be useful in regeneration of nervous system cells. Applicant further develops this assertion into a methodology for treating pathological condition or trauma requiring regeneration of nervous system cells. Accordingly, it would appear that Applicant provides a single finding (the finding), and then present an invitation to experiment to determine the effective amount, as well as routes of administration of a peptide of SEQ ID NO:8.
>
> Moreover, the instant specification provides no guidance on how to practice the claimed method with any particular pathological condition or trauma requiring regeneration of nervous system cells. A skilled artisan would not reasonably believe that administration of a peptide of SEQ ID NO:8 to a patient would lead to treatment of any pathological condition or trauma in general, as broadly claimed in claim 20.

Applicants respectfully disagree with these statements. As discussed above, the present specification provides the identity of the peptides, routes of administration, working

examples and citations to related methodologies and treatments. Applicants particularly disagree with the statement that a "skilled artisan would not reasonably believe that administration of a peptide of SEQ ID NO:8 to a patient would lead to treatment of any pathological condition or trauma in general" and request the Examiner provide reasoning or evidence to support this unsubstantiated proposition. In fact, one skilled in the art would have no reason to believe that the claimed invention would not work generally. Although the cause of the damage to nerve cells may differ and the relative potencies of the peptides may differ, the underlying mechanism of nerve death and subsequent damage is consistent for virtually all conditions resulting in nerve cell damage and no more than routine experimentation is needed to determine appropriate dosage for a given peptide of given activity. Variations in potency are simply "a matter of degree of activity," and are not a sufficient basis for finding non-enablement. *In re Bundy*, 209 USPQ 48, 51 (CCPA 1981). The "cascade of events" leading to nerve death is discussed in the declaration provided in response to the previous Office Action. Additionally, the present peptide has been shown to promote nerve growth generally and the underlying mechanism leading to this nerve growth would be expected to be consistent for nerve cells under a variety of conditions. Based upon the commonalities involved in nerve cell injury/death and regeneration, one skilled in the art would expect the present invention to be effective for regenerating nervous system cells regardless of the underlying cause.

Additionally, the Office Action Cites *Genentech v. Novo Nordisk* for the proposition that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure" and:

> when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement.

However, these vague statements from case law set forth in Office Action are never related to any of the data or guidance actually set forth in the present application. The facts of the *Genentech* case are completely inapposite to the factual predicate at hand, and the generic quotes reproduced in the rejection are clearly no more than dicta. Moreover, this quotation is not

on point because present specification not only provides the starting material, i.e. the peptide, it also provides routes of administration and targets for administration of the disclosed peptides. See, for example, page 6, lines 30-39. As such, the present invention provides much more than a "vague intimation[of a] general idea[]" or a "mere germ of an idea[.]" Instead it provides a disclosure that one skilled in the art could follow to perform the subject matter of claim 17 or 20 without undue experimentation. Therefore, the present invention is fully enabled by the present specification and applicants respectfully request the Examiner withdraw this rejection.

Claim 5 also "stands rejected 35 U.S.C. 112, second paragraph, as being indefinite for reason of record... Specifically, the metes and bounds of the recitation 'and 89-96' cannot be determined from the claim." Applicants respectfully traverse this rejection. First, the rejected phrase must be read in its proper context of a peptide "denoted SEQ ID NOS:7 and 89-96" and not in isolation. Claim 5 recites a peptide having the amino acid sequence -W-S-X_1-W-S-X_3-C-S-A_2-C-G- wherein A_2 is an amino acid sequence comprising 1 to 5 amino acids, set forth in claim 1, and X_1 and X_3 are independently selected from G, S and C. It is undisputed that one skilled in the art would readily be able to determine the metes and bounds of this claimed peptide. The only portion of the claim referred to in the rejection relates to the sequence identifiers. Because A_2 of claim 5 is defined as "comprising 1 to 5 amino acids" the sequence listing rules require sequences to be listed that include all of these variations, which are "denoted SEQ ID NOS:7 and 89-96[.]" If the skilled artisan were confused by this recitation he or she could simply refer to the sequence listing to explain any possible confusion. Moreover, "the use of sequence identifiers throughout the specification and claims, specifically, should not raise any issues under 35 U.S.C.112, first or second paragraphs." MPEP§ 2422.03. Accordingly, applicants respectfully request the Examiner withdraw this rejection.

Claim rejections 35 U.S.C. §102

Claims 5, 6, 16, 17 and 22:

> stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Gobron *et al.* for reasons of record [in the previous Office Action.] Because of the use of open language in defining the structure of the claimed peptides and because Gobron *et al.*

disclose a fragment of SCO-spondin, which has the amino acid sequence identical to SEQ ID NO:8 of the instant application and also matches the description of SEQ ID NO:7, Gobron *et al.* anticipate claims 5, 6, 7, 17 and 22.

Applicants respectfully traverse this rejection. As stated in the MPEP a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP §2131. Gobron *et al.* cannot anticipate any of the present claims because they fail to set forth each and every element of the presently claimed invention. Specifically, Gobron *et al.* fail to teach the claimed peptides having the recited termini which provides that the peptide has a comparatively short length. As set forth in the claims, the peptides of the present invention have the following structure, Y-W-S-A_1-C-S-A_2-C-G-Z, where Y and Z comprise the N- and C- terminal ends of the peptide, amino acid chains having less than 6 amino acids, or chains of compounds which are not amino acids. Accordingly, the claimed peptide has at most a contiguous amino acid chain of 26 residues (Y-W-S-A_1-C-S-A_2-C-G-Z which equal at most 5+1+1+5+1+1+5+1+1+5=26 amino acid residues). In contrast, Gobron *et al.* discloses a much longer amino acid chain length that is on the order of hundreds of amino acids. Nowhere do Gobron *et al.* disclose a peptide sequence having the recited length. Accordingly, Gobron *et al.* fail to teach each and every element of the claims and cannot anticipate the claimed invention. Therefore, applicants respectfully request the Examiner withdraw this rejection.

CONCLUSION

In view of the above remarks, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

Date November 20, 2003

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